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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/841,025	04/24/2001	Judith Aronhime	1662/52602	6176
26646	7590	06/28/2005	EXAMINER	
KENYON & KENYON ONE BROADWAY NEW YORK, NY 10004			HUANG, EVELYN MEI	
			ART UNIT	PAPER NUMBER
			1625	

DATE MAILED: 06/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/841,025

Applicant(s)

ARONHIME ET AL.

Examiner

Evelyn Huang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 April 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 161, 162, 166, 261, 262, 264, 265 and 269 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 161, 166, 262, 264, 265, 269 is/are rejected.
- 7) ☒ Claim(s) 162 and 261 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. Claims 161, 162, 166, 261, 262, 264, 265, 269 are pending. Claims 124-160, 167-260 have been canceled according to the amendment filed on 3-31-2003. Claims 263, 268, 270 have been canceled according to the amendment filed on 9-17-2004. Claims 163-165, 266, 267, 271-279 have been canceled according to the amendment filed on 4-4-2005.

#### ***Claim Rejections - 35 USC § 102***

2. The rejection under 35 U.S.C. 102(b) as being anticipated by Benincasa (5891891, PTO-1449) is maintained for the method claim 166.

Applicants contend that since claim 161 is allowable, then the method dependent thereon would also be allowable. The office did not set out a prima facie case of anticipation.

Firstly, claim 161 is not allowable. See paragraphs 5, 6 below.

Even if the particular Form D of claim 161 were allowable, the method of use thereof would not automatically be allowable for the reasons set forth in the previous office action and reiterated as follows.

The method of using the Zolpidem hemitartrate form D for treating insomnia is anticipated by the prior art method of treating insomnia with Zolpidem hemitartrate (column 2, lines 26-29) since in the in vivo physiological situation (which is mostly aqueous), the hydrate or hemiethanolate crystalline form of the zolpidem hemitartrate form D having a certain X-ray diffraction pattern no longer exist and would become identical to the the Zolpidem hemitartate of Benincasa in its use for treating insomnia.

#### ***Claim Rejections - 35 USC § 112***

3. The rejection for Claims 264-265, 269 under 35 U.S.C. 112, second paragraph is maintained for reasons of record. The 'monohydrate' of claims 264-265 or 'hemiethanolate' of claims 269, 271-272 has no antecedent basis in the base claim 161.

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Applicants argue that whether a claim is definite requires an analysis of whether one skilled in the art would understand the bounds of the claim when read in light of the specification.

However, the rejection is based on their lack of antecedent basis in the base claim 161, and not on the indefiniteness of the claims. Inserting 'which is a monohydrate or hemethanolate' after 'Form D' would obviate the rejection.

#### ***Claim Rejections - 35 USC § 112***

4. The rejection for Claims 163, 164, 266, 267, 271-278 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is rendered moot by the cancellation of these claims.

#### ***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 161, 166, 262, 264, 265, 269 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ettema I (6281360) in view of Ettema II (6242460, PTO-1449) and further in view of Brittain HG (Polymorphism in Pharmaceutical Solids. Marcel Dekker Inc. New York. 1999).

Ettema I generically discloses an imidazopyridine derivative with hypnotic and anti-anxiolytic activity (column 5, formula I; column 9, lines 7-10). A specific example, Zolpidem hemitartrate, is described (column 10, example 6).

While Ettema's example is not a monohydrate as recited in instant claims 264, 265 or a hemethanolate of instant claim 269, Ettema teaches that the Zolpidem salt can be in the form of

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a hydrate or a solvate (column 8, lines 49-50). Ettema II specifically teaches Zolpidem salt in the form of monohydrate (column 11, Example 7) or hemiethanolate (column 11, Example 9) with enhanced stability and is useful in the preparation of pharmaceutical composition for inducing sleep (column 3, lines 24-29).

At the time of the invention, guided by the teachings of Ettema I and II, one of ordinary skill in the art would be motivated to prepare the more stable monohydrate or hemiethanolate form of Zolpidem hemitartrate to arrive at the instant invention.

Ettema does not recite the 5 peaks in a X-ray diffraction pattern as in the instant claim 161, or the DTG thermogram of instant claim 262.

However, the USP general chapter on X-ray diffraction states that identity is established if the scattering angles of the ten strongest reflections obtained for an analyte agree to within + 0.20 degrees with that of the reference material, and if the relative intensities of these reflections do not vary by more than 20 percent (Brittain, page 236). The X-ray diffraction pattern having only 5 peaks with or without the DTG thermogram (which is intrinsic to the compound) as recited in the instant therefore fails to establish the identity of the polymorphic compound and is indistinguishable from the prior art compound.

6. Claims 161, 166, 262, 264, 265, 269 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benincasa (5891891, PTO-1449) in view of Kaplan (4382938, PTO-1449) and Wall, 'Pharmaceutical applications of drug crystal studies', PTO-1449) and further in view of Brittain HG (Polymorphism in Pharmaceutical Solids. Marcel Dekker Inc. New York. 1999).

Benincasa discloses Zolpidem hemitartrate for the treatment of insomnia (column 2, lines 26-30).

Benincasa does not describes the hydrate or solvate, such as hemiethanolate, as recited in the instant claims.

However, changing the form, purity or other physical characteristic of an old product does not render the new form patentable where the difference in form, purity or characteristic is inherent or rendered obvious by the prior art. Furthermore, it is well known in the art that different crystalline forms would lead to different physical and chemical properties for development of a better drug, as expressly taught by Wall (page 33, first paragraph). The

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incorporation of water would lead to hydrate and the incorporation of a solvent would lead to a solvate (page 34, first paragraph). Kaplan teaches the preparation of Zolpidem and related compounds (columns 1-2). The crystallization of the compound in ethanol has been exemplified (column 3, lines 7-8).

At the time of the invention, one of ordinary skill in the art would be motivated to prepare the hydrate or the solvate of Zolpidem as taught by Kaplan and would arrive at the instant invention with the reasonable expectation of obtaining the more desirable crystalline hydrate or solvate form of Zolpidem.

The above references do not recite the 5 peaks in a X-ray diffraction pattern or the DTG thermogram as in the instant.

However, the USP general chapter on X-ray diffraction states that identity is established if the scattering angles of the ten strongest reflections obtained for an analyte agree to within  $\pm 0.20$  degrees with that of the reference material, and if the relative intensities of these reflections do not vary by more than 20 percent (Brittain, page 236). The X-ray diffraction pattern having only 5 peaks with or without the DTG thermogram (which is intrinsic to the compound) as recited in the instant therefore fails to establish the identity of the polymorphic compound and is indistinguishable from the prior art compound.

#### ***Allowable Subject Matter***

7. Claims 162, 261 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

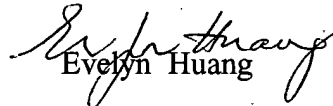
While Zolpidem hemitartrate in the form of hydrate or solvate is described by Ettema I and II, Form D with the specific X-ray powder diffraction pattern as recited in the instant claims is not taught or suggested by the prior art of record.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Evelyn Huang  
Primary Examiner  
Art Unit 1625

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